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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,875	08/13/2002	John L Teem	FSU -100C2XC1	1427

23557 7590 03/30/2006

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EXAMINER

JOIKE, MICHELE K

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/089,875	Applicant(s) TEEM, JOHN L	
	Examiner Michele K. Joike, Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13,32-57 and 60-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13,32-57 and 60-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Any rejection of record in the previous Office Action, mailed January 13, 2006 that is not addressed in this action has been withdrawn. Because this Office Action introduces new rejections other than those set forth in the previous Office Action, and are not necessitated by amendment, this Office Action is **Non-Final**.

Claim Objections

Claim 67 is objected to because of the following informalities: Claim 67 depends from itself. For purposes of examination, Examiner assumes claim 67 depends on claim 66, which is consistent with claims 62 and 63 that contain similar limitations. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33, 34 and 35 recite the limitation "said host cell" and are dependent on claim 32, which does not mention a host cell. There is insufficient antecedent basis for this limitation in the claims. This new rejection was not necessitated by amendment and is made Non-Final.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62-63, 66-67 and 69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain one CFTR polypeptide containing a $\Delta F508$ mutation, and the second CFTR polypeptide contains a mutation other than $\Delta F508$. While the Specification teaches other mutations in the CFTR polypeptides, the other mutations are in combination with $\Delta F508$. Therefore there is no mutation taught that does not include $\Delta F508$. This is a **NEW MATTER** rejection. This new rejection is necessitated by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-10, 13, 32-34, 36-41, 44-47, 49-54 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerhusen *et al.* (*J. Biol. Chem.* 247: 7627-7630, March 1999; see entire document) in view of Fields *et al.* (US 5,667,973; see entire document).

Claims 1-10, 13, 32-41, 44-54, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerhusen et al and Fields et al (as applied to claims 1-3, 5-10, 13, 32-34, 36-41, 44-47, 49-54 and 57 above), and further in view of Payan *et al.* (US 6,316,223; see entire document).

Claims 1-3, 5-13, 32-34, 36-47, and 49-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerhusen et al and Fields et al (as applied to claims 1-3, 5-10, 13, 32-34, 36-41, 44-47, 49-54 and 57 above), and further in view of Neville *et al.* (IDS reference R16; see entire document).

These rejections are maintained for the reasons set forth in the previous Office Action.

Response to Arguments Concerning Claim Rejections – 35 USC § 103 (a)

Applicant's arguments filed January 13, 2006 have been fully considered but they are not persuasive.

The following grounds of traversal are presented:

Applicant argues that according to the Zerhusen et al reference, the ordinary skilled artisan would not know which domains of CFTR are involved in dimer formation. There is no teaching to use the NBD1 domain or that the NBD1 domain is important for CFTR interaction and dimer formation. Zerhusen et al also teach the CFTR dimer to be in the head-to-tail configuration, as opposed to the tail-to-tail configuration. In fact, it is contended that Zerhusen et al teach away from the present invention because the ordinary skilled artisan would predict a head-to-tail configuration. Applicant also argues

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that there was debate in the scientific community at the time of the present invention as to whether CFTR formed monomers or dimers.

Applicant further argues that neither Payan et al nor Neville et al cure the deficiencies of Zerhusen et al. Also, as to Neville et al, applicants argue that they only teach an interaction between NBD1 and R domains.

Applicant's arguments have not been found persuasive for the following reasons. Zerhusen et al teach a CFTR dimer. Importantly, Zerhusen et al teach that intra and intermolecular interactions between CFTR polypeptides are responsible for the formation of CFTR dimers, which then form proper chloride channels (see for example the Abstract and the first paragraph of page 7627, right side). While they are assuming a head-to-tail configuration, they are not advocating it. In fact they acknowledge that more information is needed to determine which portions of the CFTR molecule are involved in the contact interaction (p. 7630). As is now known and shown by Schillers et al (as referenced in Applicants' remarks), the CFTR dimer is in the tail-to tail configuration. Although Zerhusen et al believed the dimer was in the head-to-tail configuration, it does not matter what they assumed. They showed CFTR forms a dimer, and it is inherent that it would be in the tail-to-tail configuration, as that is the way CFTR forms dimers, and therefore, NBD1 would be interacting with NBD1. There is no teaching away since Zerhusen et al acknowledge that more information is needed to determine which portions of the CFTR molecule are involved in the contact interaction.

Applicant argues that there was debate in the scientific community as to whether CFTR forms monomers or dimers. In support of this, they cite one reference from 1994.

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However, in 1998, Eskandari et al (PNAS 95:11235-11240, see specifically Abstract, p. 11239) provide evidence for the dimer conformation that Zerhusen et al teach.

Lastly applicant argues that Payan et al and Neville et al do not cure the deficiencies of Zerhusen et al. However, as shown above, there are no deficiencies of Zerhusen et al. Neville et al is used to teach that significant protein-protein interactions occur at the NBD1 domain and that NBD1 contains a $\Delta F508$ mutation.

Claims 1-3, 5-10, 13, 32-34, 36-41, 44-47, 49-54, 57, 60, 64 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerhusen *et al.* (*J. Biol. Chem.* 247: 7627-7630, March 1999; see entire document) in view of Fields *et al.* (US 5,667,973; see entire document) and in further view of Serebriiskii et al (*J. Biol. Chem.* 274: 17080-17087, 1999; see Abstract and Introduction.)

Applicant claims a method for detecting the interaction of a first CFTR polypeptide with a second CFTR polypeptide with all the limitations described previously, with the added limitation of a DNA binding domain and a transcriptional activation domain from an organism other than yeast.

Zerhusen et al and Fields et al teach all of the limitations as set forth in the prior Office Action. However, they do not teach using a DNA binding domain and a transcriptional activation domain from an organism other than yeast.

Serebriiskii et al teach a two-hybrid method performed with a LexA binding domain and a transcriptional activator for *lacZ*.

The ordinary skilled artisan, desiring to use a DNA binding domain and a transcriptional activation domain from an organism other than yeast, would have been motivated to combine the teachings of Zerhusen et al studying the interaction of a specific pair of CFTR polypeptides with the teachings of Fields et al, teaching a yeast two-hybrid assay and Serebriiskii et al, teaching a two-hybrid using a bacterial binding domain and a bacterial transactivating domain. Because Serebriiskii et al teach that use of LexA allows for effective isolation of specifically interacting protein pairs against a nonspecific background, there would be motivation to use LexA for detecting protein-protein interactions. It would have been obvious to one of ordinary skill in the art to use a bacterial binding domain and transactivating domain because they reduce the isolation of false positives. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-3, 5-10, 13, 32-34, 36-41, 44-47, 49-54, 57, 61, 65 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zerhusen *et al.* (*J. Biol. Chem.* 247: 7627-7630, March 1999; see entire document) in view of Fields *et al.* (US 5,667,973; see entire document), and Neville *et al.* (IDS reference R16; see entire document) and in further view of Brown et al (*J. Clin. Invest.* 99:1432-1444, 1997, specifically Abstract and Introduction.)

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Applicant claims a method for detecting the interaction of a first CFTR polypeptide with a second CFTR polypeptide with all the limitations described before, with the added limitation of the host cell incubated at a non-permissive temperature.

Zerhusen et al and Fields et al teach all of the limitations as set forth in the prior Office Action. However, they do not teach incubating the host cell at a non-permissive temperature.

Brown et al teach incubating a host cell containing a $\Delta F508$ mutation in CFTR at a non-permissive temperature.

The ordinary skilled artisan, desiring to detect the interaction of a first CFTR polypeptide with a second CFTR polypeptide in a host cell incubated at a non-permissive temperature would have been motivated to combine the teachings of Zerhusen et al studying the interaction of a specific pair of CFTR polypeptides with the teachings of Fields et al, teaching a yeast two-hybrid assay, Neville et al, teaching that significant protein-protein interactions occur at the NBD1 domain and that NBD1 contains a $\Delta F508$ mutation with Brown et al teaching incubating a host cell containing a $\Delta F508$ mutation in CFTR at a non-permissive temperature. Because Brown et al teach that $\Delta F508$ mutation in CFTR has folding defects that are temperature dependent and stabilized by low molecular weight compounds, there would be motivation to use temperature-sensitive cells grown at a non-permissive temperature to see whether the defective folding of other temperature-sensitive mutants can be corrected by low molecular weight compounds. It would have been obvious to one of ordinary skill in the art to use temperature-sensitive cells because they are useful for determining stabilizing

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agents for correcting certain protein folding abnormalities associated with human diseases. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER